EXCITATORY β-ADRENORECEPTORS ON ENTERAL CHOLINERGIC INTERNEURONS OF THE LARGE INTESTINE AND ILEOCECAL SPHINCTER

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Inhibitory adrenoreceptors of three types are involved in adrenergic regulation of movements of the small intestine: postsynaptic α- and β-adrenoreceptors, located on the membrane of smooth-muscle cells, and presynaptic α_2-adrenoreceptors, located on effector cholinergic neurons [12, 13]. Excitatory α-adrenoreceptors also have been found [8, 11] on the smooth muscles of sphincters of the gastrointestinal tract and, probably, of certain parts of the stomach and intestine. The question of the presence of β-adrenoreceptors on cholinergic neurons of the myenteral plexus has frequently been considered in the literature [3, 9, 10]. Our investigations [2, 4-7] have shown that excitatory β-adrenoreceptors are present in the jejunum and ileum of the cat, and are located on cholinergic interneurons of the myenteral plexus. It was accordingly suggested in the gastrointestinal tract there exists dual adrenergic control of cholinergic neurons and a specific mechanism of activation of its contractile apparatus by the sympathicoadrenal system. In the investigation described below it was shown that excitatory β-adrenoreceptors, located on cholinergic interneurons of the myenteral plexus, are present in the proximal parts of the large intestine and in the ileocecal sphincter.

EXPERIMENTAL METHOD

Cats were anesthetized with a mixture of urethane (500 mg/kg) and chloralose (50 mg/kg). Neural and humoral isolation of part of the intestine including the jejunum and ileum, the ileocecal sphincter, and the proximal part of the large intestine, was carried out. By means of a constant delivery pump the vascular bed of the isolated part of the intestine was perfused with the animal's own arterial blood. Contractile reactions of the ileocecal sphincter and the segment of large intestine were studied by means of a cuff transducer (Fig. 1), whereby the tension developed by the circular muscular layer could be recorded under isometric conditions. As the parameters of contractile activity of the regions of the intestine studied we used maximal isometric tension (expressed in mm Hg) created in the cavity of the transducer by the contracting circular muscle, and also the total contractile activity (in conventional units), estimated by the area on the tape of the automatic writer bounded by the curve tracing the contractile reaction. Details of the method were described previously [4]. The numerical results were subjected to statistical analysis by Student's test.

EXPERIMENTAL RESULTS

Isopropylnoradrenalin, injected into the vascular bed of the isolated segment of intestine in a dose of 1 or 2 μg induced contractile reactions of the intestinal segments in 31 of 45 experiments on the large intestine and in 43 of 45 experiments on the ileocecal sphincter (Fig. 2).

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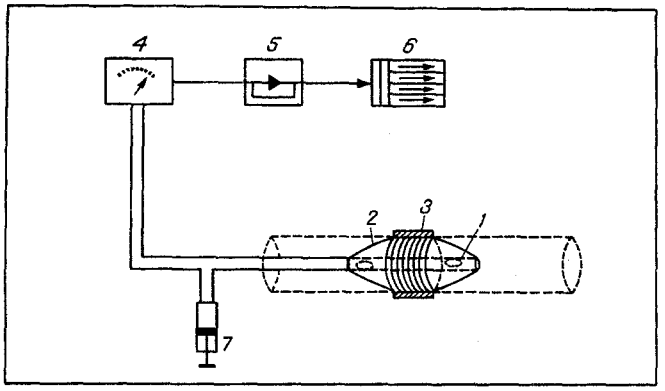

Fig. 1. Diagram of cuff transducer introduced into intestinal lumen and connected to measuring system. 1) Polyethylene tube with side openings; 2) thin rubber membrane; 3) circular muscular layer; 4) electromanometer; 5) integrating amplifier of analog computer; 6) automatic writer; 7) syringe with liquid to create pressure stretching membrane in transducer–electromanometer system.

In eight experiments we studied the effect of β-adrenoreceptor blockade by propranolol (0.3-0.4 mg/kg) on these reactions. Before the blockade, isopropylnoradrenalin evoked reactions (Fig. 2, I, 1) amounting on average to 10.4 ± 2.3 mm Hg and 4.8 ± 1.1 conventional units for the large intestine and 49.6 ± 12.1 mm Hg and 92.3 ± 21.5 conventional units for the ileocecal sphincter. During β-adrenoreceptor blockade the contractile reactions of the intestinal segments studied were not manifested (Fig. 2, I, 2).

In 11 experiments muscarinic (M) cholinergic receptors were blocked by atropine (0.2 mg/kg). In control experiments isopropylnoradrenalin caused contractile reactions of the large intestine and ileocecal sphincter (Fig. 2, III, 1), corresponding in magnitude to 16.1 ± 3.7 mm Hg and 11.2 ± 2.2 conventional unit, and 72.1 ± 4.3 mm Hg and 113.9 ± 17.7 conventional units respectively. The M-cholinergic receptor blockade led (Fig. 2, III, 2) to disappearance of the contractile reactions of the large intestine and to a sharp decrease in reactions of the ileocecal sphincter, the amplitude of which was 11.3 ± 2.3 mm Hg and 12.7 ± 3.5 conventional units. Blockade of α-adrenoreceptors by phentolamine (1 mg/kg), which was carried out in seven experiments in addition to the M-cholinergic receptor blockade in seven experiments, led to disappearance (Fig. 2, III, 3) of the atropine-resistant residue of the contractile reaction of the ileocecal sphincter, evidence of its α-adrenergic nature.

In the series of experiments with blockade of nicotinic (N) cholinergic receptors by benzohexonium (8 mg/kg) isopropylnoradrenalin caused (Fig. 2, II, 1) contractile reactions of the large intestine (six experiments) and ileocecal sphincter (nine experiments), with an amplitude of 24.0 ± 12.1 mm Hg and 28.3 ± 10.8 conventional units, and 68.5 ± 7.6 mm Hg and 101.8 ± 26.8 conventional units respectively. Against the background of the N-cholinergic receptor blockade, no contractile reactions of the large intestine and ileocecal sphincter appeared (Fig. 2, II, 2).

These experiments showed that isopropylnoradrenalin can induce contractile reactions of the large intestine and ileocecal sphincter. The connection between these reactions and β-adrenoreceptor activation is confirmed by disappearance of the effects of isopropylnoradrenalin after blockade of this type of adrenoreceptors. Abolition or considerable weakening of the contractile reactions of the large intestine and ileocecal sphincter during M-cholinergic receptor blockade points to localization of the excitatory β-adrenoreceptors on cholinergic neurons. Disappearance of the effect of isopropylnoradrenalin after N-cholinergic receptor blockade leads to the conclusion that excitatory β-adrenoreceptors are located, not on effector cholinergic neurons, but on neurons at a higher level.

The cholinergic excitatory pathway to effectors of the gastrointestinal tract includes extrapyramidal (preganglionic) cholinergic neurons and neurons of intramural ganglia (interneurons and motoneurons). The experiments described above were conducted on a preparation of a decentralized intestinal loop, in which only intramural neurons functioned. It may accordingly be concluded that excitatory β-adrenoreceptors mediating the contractile effects of isopropylnoradrenalin, are located not on parasympathetic (preganglionic) neurons, but on cholinergic interneurons.

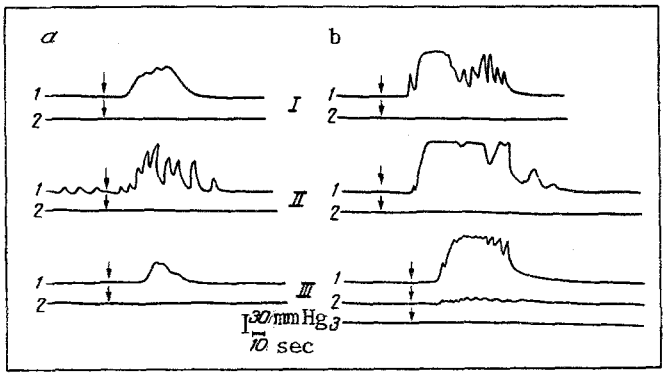

Fig. 2. Contractile reactions of large intestine (a) and ileocecal sphincter (b) induced by isopropylnoradrenalin for (1) and after (2) blockade of β-adrenoreceptors (I), nicotinic cholinergic receptors (II), and M-cholinergic receptors (III). b, III, 3 Illustrates disappearance of the atropine-resistant residue of the reaction of the sphincter after α-adrenoreceptor blockade. Arrow indicates time of injection of substance into arterial channel of perfusion pump.

Thus excitatory β-adrenoreceptors are present in the ileocecal sphincter and proximal segments of the cat large intestine, and are located on cholinergic interneurons of the myenteral plexus.

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